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(54) Title: DELIVERY SYSTEM FOR FUNCTIONAL COMPOUNDS

(57) Abstract: A delivery system for various functional compounds is disclosed. The delivery system incorporates a composition containing silica and/or alumina. Various functional materials containing particular moieties may be adsorbed onto the silica and/or alumina and used as desired. The functional compounds can be, for instance, pharmaceuticals, xenobiotics, anti-microbial agents, anti-viral agents, UV absorbers, odor control agents, fragrances, and the like. In one particular embodiment, for instance, certain dyes can be adsorbed onto the alumina surfaces. Once the dye is adsorbed onto the alumina surface, the resulting particles can be combined with a liquid vehicle for use in any suitable printing process.



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5 Background Of The Invention

In one particular application, for instance, the functional material can be a dye that is intended to be printed or otherwise applied to a substrate. In the past, various delivery systems for dyes have been proposed that are intended to facilitate application of the dye to a substrate, such as a textile material. The delivery systems, for instance, are intended to affix the dye to a substrate, prevent the dye from fading when exposed to sunlight, to prevent the dye from degrading when exposed to the environment, to facilitate application of the dye to the substrate, or, for example, to render the dye more stable.

Even in view of recent advances in the art, further improvements in delivery systems for functional materials are still needed. For example, a need currently exists for a delivery system that can bind to various functional materials that does not incorporate relatively expensive chemical formulations or that does not require any complex process steps for incorporating a functional material into the delivery system. With respect to dyes, a need also exists in the art for a delivery system for a dye that is capable of affixing the dye to negatively charged surfaces. For example, a need currently exists for a delivery system for dyes that is capable of affixing the dyes to textile materials containing natural or synthetic polymeric fibers that have a negative surface charge. With respect to pharmaceutical and nutritional materials, a need also exists in the art for a delivery system for such

materials that is capable of affixing the pharmaceutical or other health -related compounds to the delivery system. A need also exists for a delivery system that will readily and /or selectively release such pharmaceutical materials upon the occurrence of a selected event or trigger. A need also exists for a method for
5 selectively triggering the release of a pharmaceutical material or other health-related compound where and when it is needed.

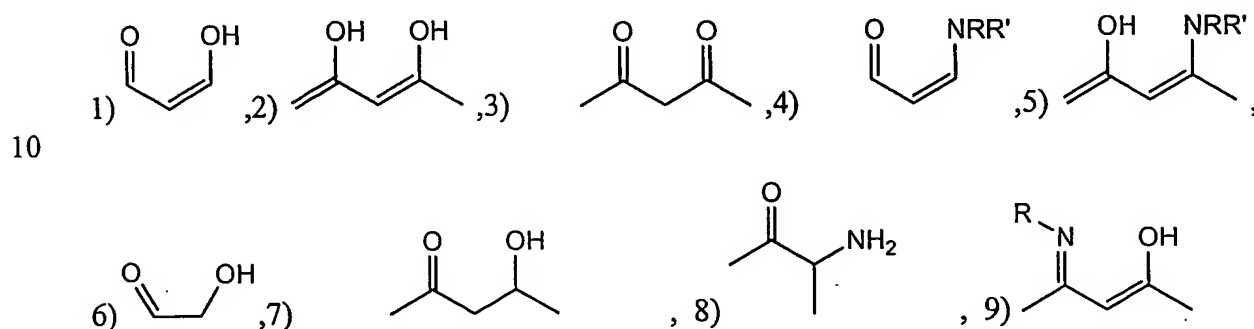
Summary Of The Invention

10 The present invention is generally directed to a delivery system for various functional materials. The functional materials can be, for instance, colorants, UV absorbers, pharmaceuticals, odor control agents, fragrances, anti-microbial agents, anti-viral agents, antibiotics, xenobiotics, nutraceutical agents (nutritional materials), and the like. In accordance with the present invention, the functional
15 materials are adsorbed onto a particle. For instance the functional materials are absorbed onto silica particles or alumina that is contained in/on a particle. The resulting particle can then be used as is or can be combined with a vehicle, such as a liquid vehicle, to deliver the functional material to a desired location. Additionally, the resulting particle, or particle containing vehicle can be
20 incorporated into a drug delivery device, such as a bandage or tampon.

For example, when the functional material is a colorant, the particles of the present invention can be incorporated into a liquid vehicle and applied to a substrate using any conventional printing means. If the functional material is a health related compound such as a pharmaceutical or nutritional compound, the
25 particles can likewise be incorporated into a vehicle and applied to a substrate such as a bandage or drug delivery device which can be placed immediately adjacent, in contact with or within a patient's body. For the purposes of this application, the term "patient's body" shall mean a human or animal body. In this fashion, the functional material can be delivered to a selected location on or within
30 a patient's body. Alternatively, such particles could be taken by a patient internally where appropriate to deliver the functional material to a desired location. In an alternative embodiment, the functional material may be triggerably released from a particle at a selected location or time, following occurrence of a triggering event,

such as exposure to a chemical, body exudates or moisture or environmental stimuli, such as a change in pH.

Thus, in one embodiment, the present invention is directed to a particle containing alumina. At least a portion of the alumina contained within the particle is present on a surface of the particle. A functional compound is bonded to the alumina on the surface of the particle. The functional compound prior to bonding with the alumina contains a moiety comprising one or more of:



a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group.

The above moieties can be present as is on a functional compound. Alternatively, however, each of the above moieties can include further R groups attached to the carbon chain shown above. In general, any such R group can appear in association with the above moieties as long as the R group does not interfere with the bonding of the moiety to an alumina.

The above moieties have been found to form a bond with alumina in constructing the compositions of the present invention. Of particular significance, it was discovered that the functional compound, in some embodiments, can bond with alumina without significantly changing the positive charge character of alumina. For example, under certain conditions, alumina may have a positive surface charge. It has been discovered that even after the functional material is bonded to the alumina, the resulting structure still maintains a positive charge. Thus, in one embodiment of the present invention, positively charged particles are formed. Due to their positive charge, the particles may be securely affixed to the surface of a substrate that carries with it a negative charge through coulombic attraction.

In one particular embodiment of the present invention, novel recording mediums, inks, and nanoparticles containing a colorant compound may be formed. In accordance with the present invention, such recording mediums, when applied to substrates, exhibit improved water and detergent resistance. For example, the delivery system of the present invention can improve the durability performance of the recording mediums especially to substrates having a negative charge. For instance, in one embodiment, a recording medium such as an ink-jet ink, can be produced according to the present invention that is substantive to substrates containing synthetic polymeric fibers, such as polypropylene fibers, polyethylene fibers, polyester fibers, and the like.

In one embodiment of the invention, the functional agent such as the pharmaceutical may be selectively released from the carrier particle (such as an alumina, silica, or alumina coated silica particle) so as to release the pharmaceutical at a targeted/desirable body location, or at a desirable moment. In one such embodiment, such selective release can be accomplished by exposure of the particle to a change in environmental condition, such as a pH change. For example, such selective release may be accomplished by exposure to an alkaline environment. Alternatively, such selective release may be accomplished by exposure to an acidic environment. Still further, such selective release may be the result of exposure of the carrier particle to particular chemical stimuli. In an alternative embodiment of the invention, a method for applying a health related compound utilizes a health-related compound coated particle, and selectively releasing the compound upon exposure of the particle to either a change in environmental condition, or upon exposure to a chemical stimuli.

The functional compounds can in one embodiment, be selectively released in either a basic or acidic environmental condition. For instance, in one specific embodiment of the invention, the functional compounds can be released in the basic/alkaline environment of a vagina experiencing a yeast infection. In a second embodiment, the functional compounds can be released in the basic environment of the small intestine so as to treat an infection, after passing through the acidic environment of the stomach. In still a further alternative embodiment, a functional compound may be released as a result of environmental stimuli as an alert or in conjunction with the completion of the delivery of a pharmaceutical material so as

to provide an indication of such delivery or the success of such treatment. Alternatively, such indicator may be released as a result of appearance of moisture or body fluids. Such indicator or signal may be in the form of a dye or fragrance. In most of these situations, while the functional compound is released, the particle
5 remains behind on a substrate, or alternatively passes through the body of the patient.

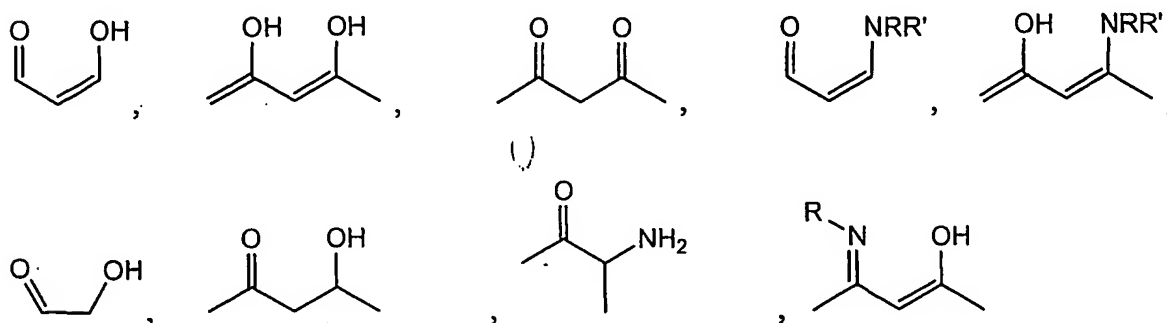
In still a further alternative embodiment, such indicator or signal may be the result of a functional material contained on a first type of particle, and such coated particle may be included with additional particles of a different variety, that contain
10 health related compounds (pharmaceutical and/or nutritional compounds). In still a further alternative embodiment, the functional material may be released in response to a particular chemical stimuli, which is intentionally applied to the site of the carrier particles. In still a further alternative embodiment, a method of utilizing a triggerably releasable delivery system in the treatment of a patient's body
15 includes the steps of providing at least one type of particle selected from alumina particles, alumina covered particles, and silica particles; adsorbing at least one health related functional compound to the surface of the particle or particles to form at least a partially coated particle or particles; exposing the at least partially coated particle or particles to a patient's body such as by ingestion, injection,
20 transdermal transfer or transmucosal transfer; and exposing the particle or particles to an environmental or chemical condition whereby the health related compound is released from the surface of the particle to the patient's body (which could be either an animal or human body). In an alternative embodiment, such health related compound is released from particles contained on a drug delivery
25 device, but because of charge attraction (as previously described) the particles themselves remain affixed to the drug delivery device.

In a further alternative embodiment of the invention, a triggerable delivery system includes a particle selected from silica, alumina or alumina coated particles; and a health-related compound adsorbed to the surface of the particle,
30 the health-related compound capable of being released from the particle upon either exposure to a change in pH, moisture, chemical stimuli, or body exudates.

In still a further alternative embodiment, the triggerable delivery system includes a particle containing alumina, at least a portion of the alumina being

present on a surface of the particle; and a health related compound adsorbed to the alumina surface of the particle, the health related compound, prior to being adsorbed with the alumina on the surface of the particle containing a moiety including at least one of

5



10 or a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group.

In still a further alternative embodiment, a drug delivery device such as a topical bandage or a tampon, includes a triggerable delivery system. The triggerable delivery system includes a particle; and a health-related compound
 15 adsorbed to the surface of the particle, with the health-related compound capable of being released from the particle upon either exposure to a change in pH, moisture, chemical stimuli, or body exudates.

Other features and aspects of the present invention are discussed in greater detail.

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Detailed Description

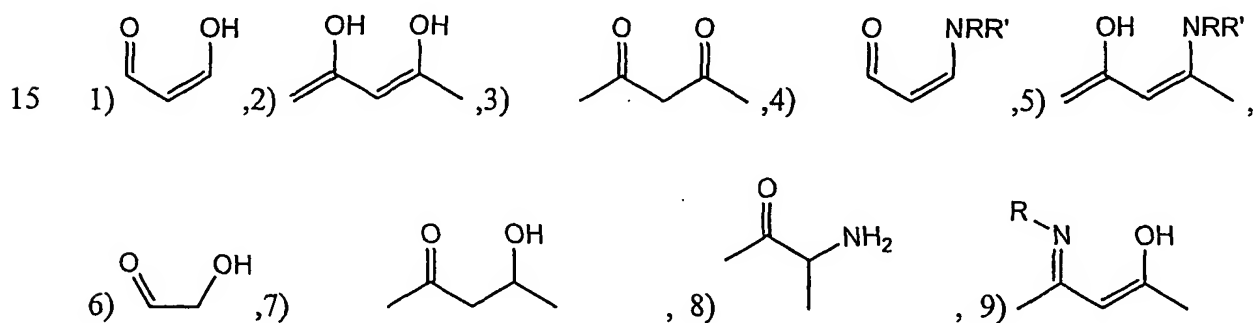
It is to be understood by one of ordinary skill in the art that the present discussion is a description of exemplary embodiments only, and is not intended as
 25 limiting the broader aspects of the present invention, which broader aspects are embodied in the exemplary construction.

In general, the present invention is directed to a delivery system for functional compounds. Functional compounds can be any suitable substance that can provide a benefit to a location once delivered. In accordance with the present
 30 invention, the delivery system is generally directed to the construction of a particle.

For example such particle may be either silica or desirably containing alumina. The alumina contained within the particle provides a bonding site on the surface of the particle for a functional compound. Specifically, the functional compound becomes adsorbed onto the surface of the alumina (or silica, if it is an entirely silica particle). Once the functional compound is bonded to the alumina, the resulting particle can then be used to deliver the functional compound to a particular location. The particles can be used as is, for instance, or can be combined with a liquid vehicle which may facilitate delivery of the particles depending upon the particular application. The particles or liquid vehicles containing the particles may further be placed within a drug delivery device such as a tampon, bandage or other transdermal delivery device.

Functional compounds that are well suited for use in the present invention include compounds that contain at least one of the following moieties:

one or more of:



a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group. As used herein, a functional equivalent to one of the above moieties refers to functional materials that include similar reactive groups as shown above, but which are not positioned on a molecule as exactly shown above and yet will still bond with alumina in a similar manner.

Referring to the moieties shown above, moiety (1) may be considered a carboxy-hydroxy moiety. Moiety (2) may be considered a hydroxy-hydroxy moiety, while moiety (3) may be considered a carboxy-carboxy moiety. Moieties (4) and (5), on the other hand, can be considered vinylalloyous amide moieties. In moieties (4) and (5) above, the amine groups can be primary amines, secondary amines, or tertiary amines. Moieties (6) and (7) may be considered hydroxyl

carbonyl moieties. Moiety (8) may be considered a carboxy amine. Moieties such as (8) may be found in amino acids. Moiety (9) may be considered a hydroxy imine. In general, any suitable functional compound containing one of the above moieties or a functional equivalent thereof may be used in accordance with the present invention. Further, it should be understood that various additional R groups may be included with the above moieties as long as the R groups do not interfere with the bond that is formed with alumina.

The present inventors have discovered that the above moieties may form a relatively strong bond to at least an alumina surface. The functional compounds may be bonded to the alumina surface in order to change the properties of the resulting particle or to perform a particular function. Without wishing to be bound by theory, it is believed that the above moieties form a bidentate ligand bonding system with alumina surfaces. For instance, it is believed that alumina forms a covalent bond and a coordinate bond with the above moieties. Further, it is believed that a surface reaction occurs causing the functional compound to remain on the surface of the particle and form a coating thereon. The functional material can cover the entire resulting particle or can be located at particular locations on the particle. Further, it should be understood that the particles of the present invention can contain more than one functional compound, or alternatively, numerous different particles can contain/include different functional compounds.

Of particular advantage, in many embodiments, it has also been discovered that a functional compound can be bonded to alumina without significantly impacting on the positive surface charge of alumina, which can be measured as zeta potential. The term "zeta potential" is used herein to mean without limitation a potential gradient that arises across an interface. This term especially refers to the potential gradient that arises across the interface between the Stern layer in contact with the particle of the present invention and the diffuse layer surrounding the particle. Zeta potential measurements can be taken using, for instance, a Zetapals instrument which are available from the Brookhaven Instrument Corporation of Holtsville, New York. For example, zeta potential measurements can be conducted by adding one to three drops of a sample into a cuvet containing 1 mM KCl solution, using the instrument's default functions preset for aqueous solutions.

Thus, once alumina is bonded to the functional material, the resulting molecule continues to maintain a relatively strong positive charge. For instance, particles made according to the present invention can have a zeta potential of greater than 20 mV, particularly greater than 30 mV, and, in some embodiments, greater than 40 mV. By remaining positively charged, the particles are well suited for being affixed to substrates that carry a negative surface charge through coulombic attraction. Depending upon the difference in charge between the particle of the present invention and the surface of a substrate, the bond of the particle in some applications can be relatively permanent and substantive. Consequently, the delivery system of the present invention can be used to affix functional compounds to various substrates without the use of chemical binders or other attachment structures. In certain circumstances, as will be discussed below, while the particle will remain affixed to a substrate, the functional compound/agent may be selectively released from the particle.

As an example, the carrier particle (delivery system) can include along its surface a pharmaceutical functional compound, and yet the particle may still retain sufficient positive charge, to allow it to be attached to a negatively charged bandage or other topically contacting substrate layer. Then upon the occurrence of a specific chemical or environmental stimuli, the functional material contained on the particle can be selectively released to the body of a patient, but the carrier particles will remain affixed to the bandage or other charged surface.

Various different particles and compositions can be used in the present invention. For instance, alumina or silica particles may be used, depending upon the functional compound and the trigger for releasing it. Silica particles are available under the designation SNOWTEX-C through from Nissan Chemical America (Houston, TX). Various different particles and compositions that contain Alumina can be used in the present invention. For example, in one embodiment, the functional material is combined with an alumina sol. Many different types of alumina sols are commercially available with varying particle size. Of particular advantage, alumina sols can be prepared that carry a relatively strong positive surface charge or zeta potential. In this embodiment, the particle that is reacted with the functional compound contains primarily and in some embodiments

exclusively alumina. Examples of alumina particle materials, include Aluminasol-100, and Aluminasol-200, available from Nissan Chemical America (Houston , TX).

In other embodiments, however, the alumina particle reacted with the functional compound can contain various other ingredients. In general, the particle
5 can contain any material that does not adversely interfere with ability of the functional material to bond to alumina. In this regard, at least a portion of the alumina contained by the particle should be present on the surface of the particle so that the alumina is available for adsorbing the functional compound.

In one particular embodiment of the present invention, the particle can
10 contain a core material coated with alumina. The alumina can form a continuous coating over the particle or a discontinuous coating. The core material can be, for instance, an inorganic oxide, such as silica. For example, in one embodiment, sols can be used that contain silica nanoparticles that have an alumina surface coating. Such sols are currently commercially available, for instance, from Nissan Chemical
15 America of Houston, Texas. The silica is coated with alumina to provide stability to the sols over certain pH ranges. In fact, alumina coated silica sols may have greater stability in some applications of the present invention in comparison to alumina sols. A specific example of alumina particle materials with silica cores, include Snowtex-AK, available from Nissan Chemical America,(Houston, TX) and
20 Ludox CI from Grace Davison, Columbia, MD.

As described above, any suitable functional compound containing one of the above moieties, a tautomer thereof, or a functional equivalent thereof may be used in accordance with the present invention. Examples of functional compounds include health related compounds such as pharmaceuticals, and xenobiotics.
25 Xenobiotics is a general term used to describe any chemical interacting with an organism that does not occur in the normal metabolic pathways of that organism. Other functional compounds can include UV absorbers, odor control agents, fragrances, therapeutic agents, nutraceutical agents, anti-viral agents, anti-microbial agents, signal agents and the like. One example of a therapeutic agent
30 that may be used in the present invention is hydrocortisone. Examples of nutraceutical agents include ascorbic acid and aspartame. In one particular embodiment, the functional compound may be tetracycline, which is a known antibacterial agent.

In still another embodiment of the present invention, the functional compound can be a colorant, such as dye. Particular examples of dyes that may be used in accordance with the present invention are discussed in greater detail below.

5 Once any of the above-mentioned functional compounds are bound to alumina (or silica as the case may be), the particle acts as a delivery vehicle for delivering the functional compound to a desired location. Once bound to the particle, the functional compounds may be easier to handle, may be more stable, or may have other improved properties depending upon the application. Further,
10 the resulting particle structure can be incorporated into various other mediums. For instance, the particle structure can be incorporated into liquid vehicles, can be formed into capsules, can be combined with gels, pastes, other solid materials, and the like. As previously stated, the particles can also be incorporated into drug delivery devices such as bandages and tampons.

15 The particles formed according to the present invention and the functional compound, can be present in various forms, shapes, and sizes depending upon the desired result. For instance, the particles can be of any shape, for example, a sphere, a crystal, a rod, a disk, a tube, or a string of particles. The size of the particle can also vary dramatically. For instance, in one embodiment, the particles
20 can have an average dimension of less than about 1 mm, particularly less than about 500 microns, and more particularly less than about 100 microns. In other embodiments, however, even smaller sizes may be desired. For instance, the particles can have an average diameter of less than about 1,000 nm, and particularly less than about 500 nm. As used herein, the average dimension of a
25 particle refers to the average length, width, height, or diameter of a particle.

As described above, the particles of the present invention include a surface layer that contains one or more functional compounds. The coating on the particle can be continuous or discontinuous. The particle itself is believed to be amorphous.

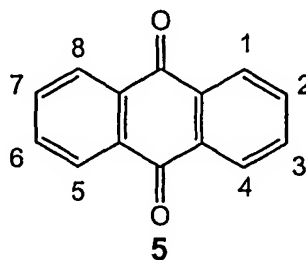
30 In one particular embodiment, the present invention is directed to a delivery system for dyes. In particular, it has been discovered that the use of alumina as described above provides various advantages and benefits when attempting to apply a dye to a substrate. For instance, it has been discovered that the alumina

delivery system can provide a means to make permanent prints onto substrates having negatively charged surfaces, such as substrates containing thermoplastic polymers as well as natural fibers. The ink becomes affixed to the substrate at relatively low cost and low complexity without the use of chemical binders and without the use of a pre-treatment or post-treatment process on the substrate.

For example, once a dye is adsorbed onto alumina in accordance with the present invention, for many applications, the resulting particle has a positive charge. Thus, the particle can be affixed to negatively charged surfaces through coulombic attraction. Depending upon the charge difference between the particles and the substrate, the dye may exhibit permanent properties such as wash fastness by being resilient to water and detergents. For example, generally wash fastness can be obtained if the charge difference between the substrate and the particle is greater than about 42 mV.

In general, any dye containing a carbonyl-hydroxy moiety, a hydroxy-hydroxy moiety, a carbonyl-carbonyl moiety, a vinylalagous amide moiety, a tautomer thereof, or a functional equivalent thereof as described above, or any of the other moieties, may be used in the process of the present invention. Various examples of dyes that may be adsorbed onto alumina are as follows. It should be understood, however, that the below list is not exhaustive and is not intended as limiting the invention.

Dyes containing the Anthraquinone (5) Chromophore:



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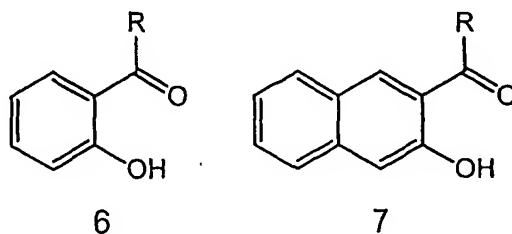
Numbers indicate the substitution positions of the anthraquinone structure. This table indicates dye substituents that occur at positions 1, 4, 5, or 8 on the anthraquinone structure. In other words, this table shows the presence of groups that form alumina bonding moieties 1 through 5.

30

Name	Substituent at position 1 or 4 or 5 or 8	Other groups present include
CI Acid Black 48	NH ₂	SO ₃ Na
CI Acid Blue 25	NH ₂	SO ₃ Na
CI Acid Blue 40	NH ₂	SO ₃ Na
CI Acid Blue 41	NH ₂	SO ₃ Na
CI Acid Blue 45	OH, NH ₂	SO ₃ Na
CI Acid Blue 129	NH ₂	SO ₃ Na
CI Acid Green 25	NHAr	SO ₃ Na
CI Acid Green 27	NHAr	SO ₃ Na
CI Acid Green 41	OH, NHAr	SO ₃ Na
CI Mordant Red 11 (Alizarin)	OH	
CI Mordant Black 13 (Alizarin Blue Black B)	OH, NHAr	SO ₃ Na
Alizarin Complexone (Aldrich 12,765-5)	OH	
CI Mordant Red 3 (Alizarin Red S)	OH	SO ₃ Na
CI Natural Red 4 (Carminic Acid)	OH	COOH
CI Disperse Blue 1	NH ₂	
CI Disperse Blue 3	NH(alkyl)	
CI Disperse Blue 14	NHCH ₃	
Emodin (6-methyl-1,3,8-trihydroxy anthraquinone)	OH	
Nuclear Fast Red (Heliofast Rubine BBL)	OH, NH ₂	SO ₃ Na
CI Natural Red 16 (Purpurin)	OH	
CI Natural Red 8	OH	
Quinalizarin	OH	
Quinizarin	OH	
CI Reactive Blue 2	NH ₂ , NHAr	SO ₃ Na
Solvent Green 3	NHAr	

Dyes Containing Salicylate, or 3-hydroxy-2-naphthoic acid moieties.

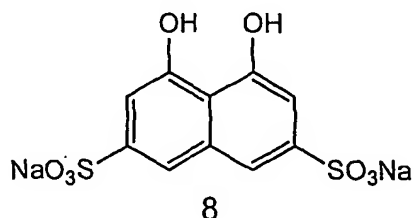
- Dyes containing salicylate (6, R=OH), Salicamide (6, R=NH₂, NHAr, NHAlk), or BON acid (3-hydroxy-2-naphthoic acid) (7, R=OH) or a nitrogenous BON acid derivative (7, R=NH₂, NHAr, NHAlk) moiety as shown below may also be used in accordance with the present invention. These dyes often fall into the Colour Index Mordant application class.



Colorant	Substantive Group	Chromophore
Aluminon (tri ammonium salt) (Aurintricarboxylic acid) (CI Mordant Violet 39 is the trisodium salt)	Salicylate	TPM
CI Mordant Blue 29	Salicylate	TPM
CI Mordant Blue 3 (Chromoxane Cyanine R)	Salicylate	TPM
Calconcarboxylic acid 3-hydroxy-4-(2-hydroxy-4-sulfo-1-naphthylazo)- -2-naphthalenecarboxylic acid	BON acid	Azo
CI Mordant Orange 1 (Alizarin Yellow R)	Salicylate	Azo
CI Mordant Orange 6 (Chrome Orange GR)	Salicylate	Azo
CI Mordant Orange 10	Salicylate	Azo
CI Mordant Yellow 7	Salicylate	Azo
CI Mordant Yellow 10	Salicylate	Azo
CI Mordant Yellow 12	Salicylate	Azo
CI Mordant Green 31 (Naphtho Chrome Green)	BON Acid	Azo
CI Azoic Coupling Component 2 (Naphthol AS)	Arylamido BON acid	N/A
CI Azoic Coupling Component 45 (Naphthol AS B1)	Arylamido BON acid	N/A
3-hydroxy-2-naphthoic acid (BON Acid)	BON Acid	N/A
Xylidyl Blue 1	Aryl amido BON acid	Azo

Dyes Based Upon Chromotropic Acid.

- 5 Dyes based upon Chromotropic acid **8** are also substantive to alumina. Azo dyes are formed when chromotropic acid is reacted with a diazonium salt. Azo coupling occurs at positions 2 and / or 7.



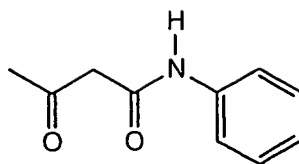
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Colorant
CI Acid Red 176 (Chromotrope 2B)
CI Acid Red 29 (Chromotrope 2R)
Plasmocorinth B
Sulfonazo III (3,6-Bis(2-sulfophenylazo)-4,5-dihydroxy-2,7-naphthalene disulfonic acid sodium salt)
2-(4-sulfophenylazo)-1,8-dihydroxy-3,6-naphthalenedisulfonic acid

Dyes Containing Acetoacetanilide

- 15 Dyes containing acetoacetanilide moieties **9** also contain the correct geometry to bond to alumina. Azo dyes couple to acetoacetanilide beta to the two carboxyl groups. An example is CI Acid Yellow 99, **10**. Acetoacetanilide will adsorb onto

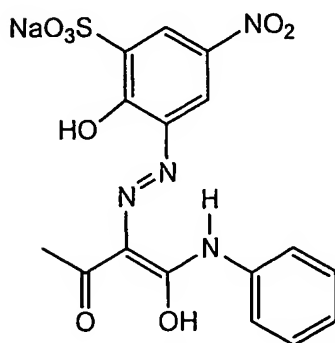
the surface of alumina.



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Acetoacetanilide

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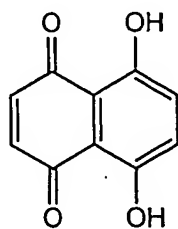
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CI Acid Yellow 99

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Naphthoquinone Colorants:

Naphthoquinone (11) type Structures are also useful for forming complexes with the surface of alumina:



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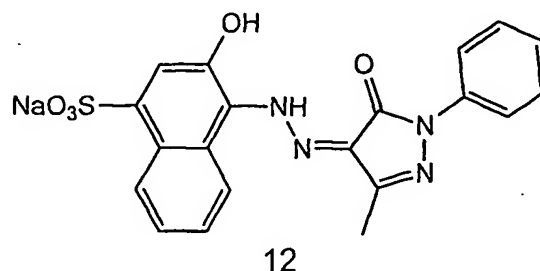
CI Natural Black 1 (Hematoxylin) is another example of a dye that contains quinoid groups and is substantive to alumina.

20 Aluminum Dyes; Dyes Known to be Useful for Staining Anodized Aluminum.

There are several dyes that are known to be useful for the coloration of anodized aluminum, including CI Mordant Red 7 (Eriochrome Red B), 12. It is believed that the geometry of the five membered pyrazolone ring oxygen atom brings it into the correct position with the beta-naphthol group for complexation with alumina. Thus, the following structure can be considered a functional

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equivalent to a carbonyl-hydroxy moiety. The structure also contains an iminalogous amide moiety, which is functionally equivalent to a vinalogous amide.

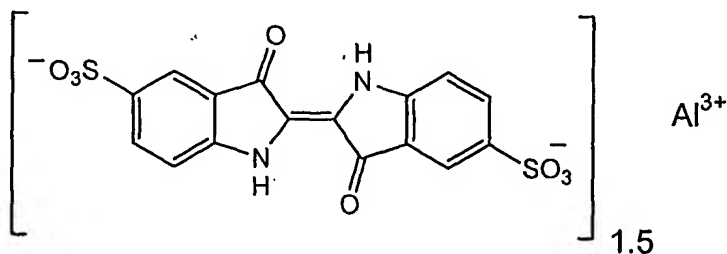


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Aluminum Lake Forming Dyes:

Certain anionic dyes may be precipitated using certain metal ions to form insoluble colored compounds known as Lake Pigments. For example, Erythrosine (Tetraiodofluorescein) forms an insoluble salt with aluminum ions. The salt is known as CI Pigment Red 172.

CI Pigment Blue 36 is the aluminum lake of indigo disulfonate (FD+C Blue 1):



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In addition to a dye as described above, in some embodiments, it may be desirable to bond other functional compounds or additives to the alumina. For instance, additives that assist in the dyeing process or that stabilize the dye may also be bonded to the alumina if the additive contains a moiety as described above. Such functional additives that may be used include charge carriers, thermal oxidation stabilizers, crosslinking agents, plasticizers, a charge control additive, a flow control additive, a filler, a surfactant, a chelating agent, a colorant stabilizer, or a combination thereof.

Various methods can be utilized to construct dye particles in accordance with the present invention that contain a dye adsorbed onto alumina. For instance,

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in some applications, the alumina and the dye containing a reactive moiety can be combined and reacted in an aqueous solution.

In some embodiments, however, the dye may be difficult to dissolve in water. In this embodiment, the dye can first be dissolved in a minimum quantity of a solvent. The solvent can be, for instance, acetone, ethanol or a similar liquid that is miscible with water. After the dye is combined with the solvent, if desired, a surfactant can be added in an amount greater than about 0% to about 50% by weight of dye solids added. In general, the amount of surfactant added to the solvent should be minimized. One suitable surfactant that can be used, for instance, is SURFYNOL 440 surfactant sold by Air Products and Chemicals, Inc. located in Allentown, Pennsylvania.

With rapid stirring, the dissolved dye solution can then be added to a dilute aqueous suspension that contains particles comprising alumina. Although not critical, better results may be achieved if the aqueous suspension is slightly heated.

After constant stirring for a sufficient amount of time, the dye disperses by precipitation throughout the mixture and slowly dissolves into the water. Once dissolved into the water, the dye can be adsorbed by the alumina contained in/on the particles.

Once the dye is adsorbed onto the alumina, the resulting particles can be used to formulate a suitable colorant composition for use in various processes, such as in a suitable printing process.

The colorant composition may comprise an aqueous or non-aqueous medium, although an aqueous medium is useful for applications which employ liquid printing mediums. The colorant compositions of the present invention contain particles, as well as, desirable colorant stabilizers and additives. For example, the colorant composition may contain the above-described particles in combination with any of the following additives: a second colorant; a colorant stabilizer, such as a porphine; a molecular includant; a pre-polymer; and any additional components as described above.

The present invention encompasses recording mediums such as ink jet inks comprising the nanoparticles disclosed herein. Inks used in ink jet printers are described in U.S. Patent No. 5,681,380, assigned to Kimberly-Clark Worldwide,

Inc., which is incorporated herein by reference in its entirety. Ink jet inks will usually contain water as the principal solvent, preferably deionized water in a range of between about 20 to about 95 percent by weight, various co-solvents in an amount of between about 0.5 and about 20 percent by weight, and the particles of the present invention.

Various co-solvents may also be included in the ink formulation. Examples of such co-solvents include a lactam such as N-methyl pyrrolidone. However, other examples of optional co-solvents include N-methylacetamide, N-methylmorpholine-N-oxide, N,N-dimethylacetamide, N-methyl formamide, propyleneglycolmonomethylether, tetramethylene sulfone, and tripropyleneglycolmonomethylether. Still other solvents which may be used include propylene glycol and triethanolamine (TEA). If an acetamide-based cosolvent is also included in the formulation it is typically present at about 5 percent by weight, within a range of between about 1.0-12 percent by weight.

Optionally, one or more humectants in an amount between about 0.5 and 20 percent by weight may be included in the ink formula. Additional humectants for optional use in the formulation include, but are not limited to, ethylene glycol, diethylene glycol, glycerine, and polyethylene glycol 200, 400, and 600, propane 1,3 diol, other glycols, a propyleneglycolmonomethyl ether, such as Dowanol PM (Gallade Chemical Inc., Santa Ana, CA), polyhydric alcohols, or combinations thereof.

Other additives may also be included to improve ink performance, such as a chelating agent to sequester metal ions that could become involved in chemical reactions that could spoil the ink over time, for example for use with metal complex dyes, a corrosion inhibitor to help protect metal components of the printer or ink delivery system, a biocide or biostat to control unwanted bacterial, fungal, or yeast growth in the ink, and a surfactant to adjust the ink surface tension. However, the use of a surfactant may be dependent on the type of printhead to be used. If a surfactant is included, it is typically present in an amount of between about 0.1 to about 1.0 percent by weight. If a corrosion inhibitor is included, it is typically present in an amount between about 0.1 and about 1.0 percent by weight. If a biocide or biostat is included, it is typically present in an amount between about 0.1 and about 0.5 percent by weight.

If a biocide or biostat is added to the ink formulation, it may be exemplified by Proxel GXL (Zeneca Corporation, Wilmington, Delaware). Other examples include Bioban DXN (Angus Chemical Company, Buffalo Grove, Illinois). If a corrosion inhibitor is added to the formulation, it may be exemplified by Cobrattec (PMC Specialty Group Distributing of Cincinnati, Ohio). Alternate corrosion inhibitors include sodium nitrite, triethanolamine phosphate, and n-acyl sarcosine. Still other examples include benzotriazole (Aldrich Chemical Company, Milwaukee, Wisconsin). If a surfactant is included in the formulation, it is typically a nonionic surfactant exemplified by Surfynol 504 (Air Products and Chemicals, Inc., Allentown, Pennsylvania). Still other examples include Surfynol 465, and Dynol 604 also available from Air Products. If a chelating agent is included in the formulation it may be exemplified by an ethylene diaminetetraacetic acid (EDTA). Other additives such as pH stabilizers/buffers, (such as citric acid and acetic acid as well as alkali metal salts derived therefrom), viscosity modifiers, and defoaming agents such as Surfynol DF-65, may also be included in the formulation, depending on the product application.

Depending upon how the colorant composition is formulated, the composition can be used in various printing processes. For instance, in addition to ink jet printing and other non-impact printers, the colorant composition can be used in screen printing processes, offset lithographic processes, flexographic printing processes, rotogravure printing processes, and the like. In some of the above printing processes, a thickener may need to be added to the colorant composition. The thickener can be, for instance, an alginate.

The recording medium or colorant composition of the present invention may be applied to any substrate to impart a color to the substrate. The substrate to which the composition is applied may include, but is not limited to, paper, wood, a wood product or composite, woven fabrics, non-woven fabrics, textiles, films, plastics, glass, metal, human skin, animal skin, leather and the like. In one aspect, the colorant composition or recording medium may be applied to textile articles such as clothing.

In one particular embodiment, a colorant composition containing particles of the present invention may be applied to a substrate having a negative surface charge. As described above, the alumina contained in the particles of the present

invention retain a positive charge even after adsorption of a dye. Consequently, the particles remain affixed to negatively charged surfaces. In fact, wash durability of the colorant composition may occur if there is a substantial amount of charge difference between the substrate and the particles of the present invention.

5 In view of the above, colorant compositions made according to the present invention are particularly well suited to being applied to natural and synthetic substrates that have a negative surface charge. For instance, naturally occurring materials that generally contain a negative surface charge include cotton fibers, cellulose fibers, and substrates made therefrom. Such substrates include all types
10 of fabrics, garments and apparel, paper products, and the like.

In addition to the above natural materials, in one particular embodiment, colorant compositions made according to the present invention have been found to be well suited to being applied to substrates made from synthetic polymers, such as thermoplastic polymers. Such substrates can include, for instance, woven and
15 non-woven materials made from a polyolefin polymer such as polypropylene or polyethylene, polyester, and the like. In the past, various problems have been experienced in trying to affix dyes to these types of materials. Consequently, either complicated dye structures have been used or dyes and or pigments have been applied in conjunction with chemical binders. The particles of the present
20 invention, however, can permanently affix to these materials without the use of chemical binders or complex chemical constructions.

Although not needed, in some embodiments it may be desirable to pre-treat or post-treat the polymer substrates which may further serve to affix the dyes or other functional compounds described to the materials. For instance, substrates
25 made from synthetic polymers can undergo a pretreatment process for increasing the negative surface charge. For example, such pretreatment processes include subjecting the substrate to a corona treatment or to an electret treatment. An electret treatment, for instance, is disclosed in U.S. Patent No. 5,964,926 to Cohen, which is incorporated herein by reference in its entirety. Such
30 pretreatments have been found not only to increase the negative surface charge of polymeric materials, but also assist in wetting out the polymer and enhancing surface adhesion between the polymer and the particles of the present invention.

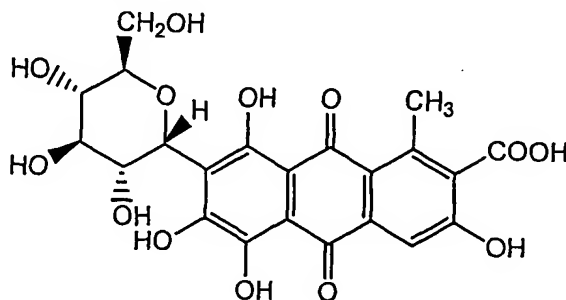
In addition to pretreatment processes, substrates contacted with the particles of the present invention can also undergo various post treatment processes which further serve to affix the particles to the substrate. For example, in one embodiment, the treated substrate can be subjected to radio frequency radiation or to microwave radiation. Alumina is known to adsorb radio frequency radiation and microwave radiation causing the particles to heat. Once heated, it is believed that the particles become further embedded into the polymeric substrate. Further, the particles can be heated without also heating the substrate to higher than desired temperatures.

In addition to the foregoing embodiments, functional compounds (health-related compounds) may be adsorbed to the described particles and then either utilized while on the particles to treat a condition or symptoms, or selectively released from the particles to treat medical conditions or symptoms. Such selective release can be accomplished via an environmental trigger or chemical stimuli. Such coated particles can be applied topically to a patient's body either directly, or with the assistance of a drug delivery device, such as a modified bandage, tampon, or other known transdermal delivery apparatus. Alternatively, such coated particles may be taken internally through various mechanisms.

The present invention may be better understood with respect to the following examples.

Example 1

Aluminasol 200 (Nissan Chemical America) was diluted with DI water to give a 2% Aluminasol 200 suspension. Meanwhile, carminic acid (0.02g) was suspended in DI water (1g). Carminic acid includes hydroxy-carbonyl moieties and can be represented as follows:



Carminic Acid

The zeta potential of alumina particles in the Aluminasol was monitored as carminic acid was dripped into the measurement cell. The zeta potential did not change as more carminic acid was added. A significant color shift was observed as the carminic acid (red / orange) was added to the Aluminasol (bluish magenta).

5 The following zeta potential results were obtained:

	Zeta Potential
2% Aluminasol	56.70 mV
10 Aluminasol + 2 Drops Carminic	49.27 mV
Aluminasol + 5 drops carminic	56.68 mV
Aluminasol + 7 drops carminic	58.59 mV

As shown above, the positively charged alumina was capable of adsorbing carminic acid without going through a charge reversal step.

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Example 2

Aluminasol 200 (Nissan Chemical America, 2 g) was diluted with DI water (98g) with good stirring. Carminic acid (Aldrich, #22,925-3) (0.5011g) was suspended in DI water (23.7135 g) with good stirring. The carminic acid did not dissolve completely at this concentration, and so whenever portions were taken, they were taken while stirring vigorously so that suspended solids were also withdrawn. A hypodermic syringe was used to withdraw 1. ml of carminic acid suspension. This was added to the diluted Aluminasol 200 with good stirring. The suspension changed from a white to a bluish red.

25 The Zeta potential was monitored after addition to check for changes as follows:

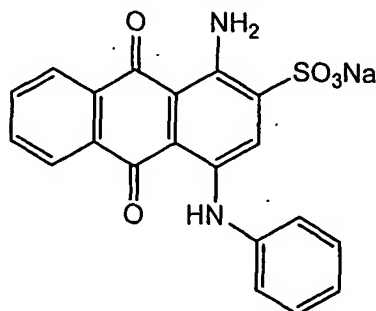
	Zeta Potential
30 Initial (2% Aluminasol)	+55.70mV
2 min after carminic acid addition	+45.08mV
5 min after carminic acid addition	+45.68mV

This mixture was allowed to stir overnight. The next morning, all dye had dissolved, and no dye crystals were observed.

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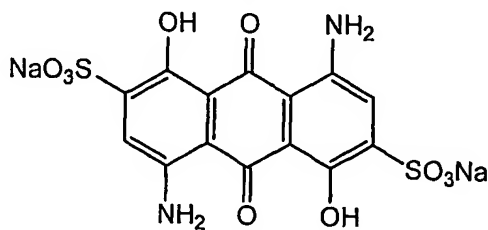
Example 3

In this example, in addition to carminic acid, Cl Acid Blue 25 and Cl Acid Blue 45 were bonded to alumina in accordance with the present invention. Cl Acid Blue 25 and Cl Acid Blue 45 have the following structures:



Cl Acid Blue 25

0.2008 g Cl Acid Blue 25 (Aldrich) was added to 19.7735 g DI water and stirred to give a suspension, which was stirred for 30 minutes. 1 ml of this was added to a mixture containing 2g Aluminasol and 98g DI water. Mixture stirred overnight to ensure that all dye had dissolved.



Cl Acid Blue 45

0.2507 g of Cl Acid Blue 45 (Aldrich) was suspended in 20.1751g DI water with stirring for 30 minutes. 1ml (syringe) was added to a mixture of 2g Aluminasol and 98g of DI water to give a blue complex. Mixture stirred overnight to ensure that all dye dissolved.

In the following sample, a high concentration of Aluminasol 200 was combined with carminic acid. Specifically, 0.111g glacial acetic acid (Fischer, ACS plus reagent grade) was diluted with 29.795g DI water. This was added to 49.941g of Aluminasol 200, slowly with good stirring. This mixture was stirred for 20 mins, at which point, 4ml (measured using a syringe) of a suspension of carminic acid in DI water (0.5011g carminic acid in 23.7135g water) was added at once, with good stirring. Mixture stirred overnight.

A fourth sample was then constructed containing the same ingredients (carminic acid) in the same amounts as listed in Example 2 above.

All mixtures appeared to be homogeneous in that upon standing for three hours, no sludge settled out, and no dark dye crystals were observed. Zeta potentials and particle size analysis were conducted using a Brookhaven Instrument PALS Zeta potential analyzer for all the samples except the sample containing CI Acid Blue 25. The following results were obtained:

System	Zeta Potential	Mean Diameter	Half Distribution Width
2% Aluminasol / Acid Blue 45	+40.69 mV	333.5nm	94.7nm
2% Aluminasol / Carminic Acid	+45.14 mV	300.6nm	139.5nm
50% Aluminasol/ Carminic Acid	+43.73 mV	347.3nm	181.6nm

The above three solutions were then subjected to a dialysis test to demonstrate that the dye was adsorbed onto the alumina surfaces. Specifically, the three solutions were dialyzed against 3% glacial acetic acid using Sigma Dialysis Tubing (Cellulose, 12,000mw cut off, Sigma D-0655. Tubing was soaked in DI water for two hours prior to use to remove glycerine, and to make the tubing flexible.) As a control, a small amount of carminic acid was added to a dialysis tubing and placed in a bath containing 3% acetic acid. Within 2 hours, carminic acid had traversed the cellulose membrane and had colored the 3% acetic acid solution. No color was observed from the aluminasol mixtures, suggesting, along with the color change, that the colorant was strongly sorbed by the particles. The next morning, the 50% aluminasol / carminic acid solution had colored the water bluish red. However, it is believed that the bag had ruptured. Also, a very faint, almost indiscernible blue coloration was noticed in the dialysis solution of the aluminasol acid blue 45 dialysis, suggesting that this colorant did not as strongly adsorb into the alumina.

Example 4

The following tests were conducted to demonstrate the washfastness of the particles of the present invention on cotton.

The three compositions prepared in Example 3 above containing 2% aluminasol/Acid Blue 45; 2% aluminasol/carminic acid, and 50%

aluminasol/carminic acid were spotted onto cotton poplin fabric (0.01198g/cm², from Yuhan-Kimberly, uncoated) and dried overnight at 60°C. As the aluminasol containing mixtures were dropped onto the cotton, it was observed that only the flooded area of the fabric took up color. Colorless water wicked out from around the spotted area suggesting that i) no unadsorbed dye was present in the mixture, and ii) the nanoparticles sorbed onto the cotton, and were immobilized.

A control sample was also prepared. In particular, a carminic acid solution was first formulated containing 0.5011 grams of carminic acid in 23.7135 grams of DI water. The carminic acid solution was dropped onto cotton poplin fabric using a pipette and allowed to dry overnight at 60°C.

Samples were washed by i) rinsing under a hot running tap, and then by stirring for 2 hours in 2 liters of water containing 1 g / liter Aerosol OT (dioctyl sodium sulfosuccinate surfactant obtained from Cytec Industries of West Patterson, New Jersey) and 1 g / liter of sodium bicarbonate, with stirring (mechanical paddle stirrer). Samples were entered into the washing bath at 60°C, and the bath cooled over two hours to 30°C. The fabric was rinsed in cold water, then dried in the air at ambient.

The Carminic acid of the control sample rinsed out of the cotton. Almost all of the dye / Aluminasol complex remained as a bluish-red stain.

Example 5

The following tests were conducted to demonstrate the washfastness of particles made according to the present invention on a polypropylene non-woven spunbond fabric. The spunbond fabric tested had a basis weight of 2 osy.

Polypropylene spunbond was smeared with i) carminic acid, ii) the concentrated 50% Aluminasol / carminic acid complex suspension prepared in Example 3 and iii) the 2% Aluminasol / carminic acid complex suspension prepared in Example 3. In all cases, the polypropylene was difficult to wet out with these materials, and so smearing was required using a rubber-gloved finger and the teat pipette used to apply the liquids. Once the material had been smeared on forcibly, the material showed little retraction. The samples were allowed to dry overnight at 60°C.

More polypropylene was smeared with the 50% Aluminasol / carminic acid complex. These samples were dried at 60°C and then cut in half. Half of the samples were subjected to microwave radiation (Sharp carousel domestic microwave oven, model # R-410 CK, output 1100 Watt) for a range of times. (10
5 seconds, 20 seconds, 28 seconds)

All polypropylene samples were washed using the same procedure as for the cotton in Example 4 above. The following results were obtained:

i) Carminic acid of the control sample rinsed out of the PP.
ii) Some, but not all of the aluminasol / carminic acid inks were retained
10 on the polypropylene. The nature of the washing out was not a general fading of the area. However, there appeared to be a loss of all material from certain areas, but not others. In other words, it looked as though the ink had not wet out the polypropylene.

iii) Considerably more aluminasol / carminic acid was retained on
15 samples that were microwaved prior to washing. It is thought that the microwave treatment may have heated the colored particles, allowing them to embed in the polypropylene. Microwaving for longer time did not considerably improve the washfastness of the prints.

20

Example 6

In this example, instead of using an alumina sol, a sol containing silica particles that had an alumina surface coating were used. The surface coated silica suspension was obtained from Nissan Chemical America of Houston, Texas. The
25 suspension is sold under the trade name SNOWTEX-AK.

50ml of 20% wt/wt suspension of SNOWTEX-AK (Nissan Chemical America, Houston, Texas) was stirred at ambient temperature while 0.2 grams of carminic acid dye (Aldrich Chemical Company, Milwaukee, Wisconsin) was added. Stirring was continued overnight and resulted in a dramatic color change from
30 blood red to blue/purple.

The physical parameters of the nanoparticles are:

SNOWTEX-AK - Size: 62 nm and Zeta Potential: +36mV.
SNOWTEX-AK with carminic acid - Size: 83 nm and Zeta Potential: +35mV.

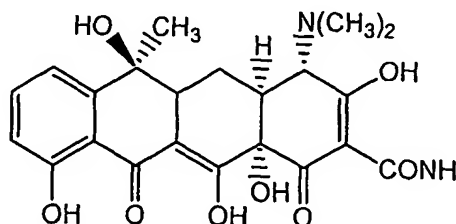
The bond formation of the aluminum-dye complex did not result in a change in zeta potential.

The above "ink" solution was applied to 4" x 4" pieces of untreated cotton fabric and allowed to air-dry. A similar control sample was constructed using only carminic acid. The dried fabrics were then subjected to a washing cycle in 2litres of water containing Ajax liquid detergent and sodium bicarbonate at 60°C for 2 hours. The fabric samples were then air-dried. The SNOWTEX-AK/carminic acid sample did not loose any color after the washing cycle. In contrast, the control sample (a sample stained with 0.2 g Carminic Acid in 50 ml water, dried under the same conditions) lost all of the color upon washing under the same conditions.

Example 7

The following example demonstrates the application of the present invention to other functional compounds as opposed to dyes.

5 Tetracycline is an antibacterial agent that contains a carbonyl-hydroxy function capable of bonding with alumina in accordance with the present invention. Tetracycline is a series of isomers of cyclomycin. Tetracycline contains as a principle component the following:



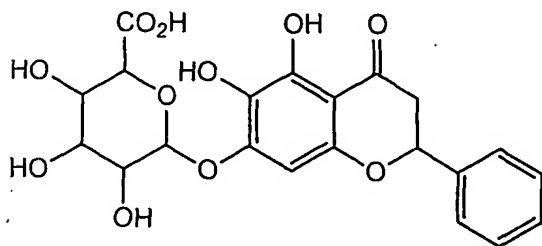
10 4S-(4,4,5,6,12)-4-(dimethylamino)-1,4,4,5,5,6,11,12-octahydro-3, 6,10,12,12-pentahydroxy-6-methyl-1, 11-dioxo-2-naphthacenecarboxamide.

The UV-visible absorbance spectrum of Tetracycline was measured using a UV-visible spectrophotometer (Perkin-Elmer UV-Visible spectrophotometer.) Tetracycline was found to absorb at 357nm in water. When SNOWTEX AK
15 suspension (as described in Example 6) was added to the tetracycline solution, a bathochromic shift occurred to give an absorbance of 365 nm, suggesting that the tetracycline had adsorbed onto the alumina surface of SNOWTEX AK particles.

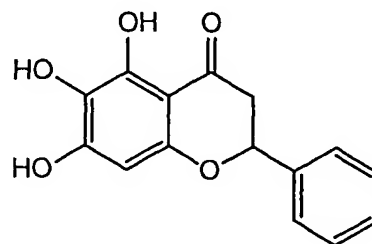
Further Pharmaceutical Examples

20 In further Examples, additional pharmaceutical agents were evaluated for their propensity to bind strongly to alumina particles. They included the agents described in the following table, and which demonstrated the noted shift. These agents are considered antineoplastic for use as drugs that kill or stop the spread of cancer cells. Baicalein has been studied for its antiproliferation effect of human T-lymphoid leukemia cells.

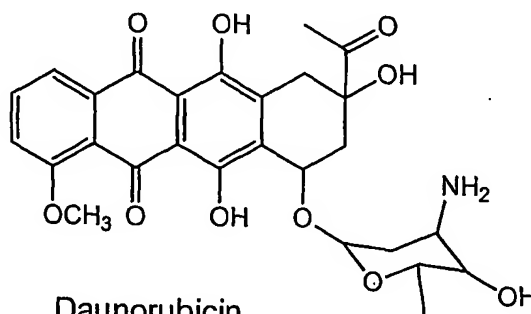
SAMPLE	UV-VIS. ABSORPTION (nm)	
	FREE AGENT	SN-AK / AGENT
Baicalin Hydrate	278 and 322	295 and 388
Baicalein	320	348
Daunorubicin	472	480



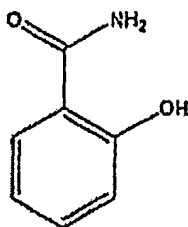
Baicalin Hydrate

Baicalein
(Astringent)

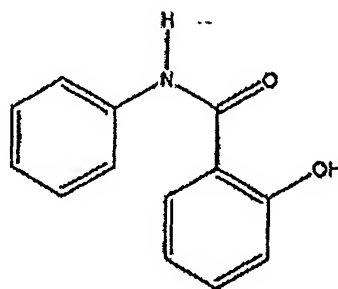
5 17

Daunorubicin
(Antineoplastic)

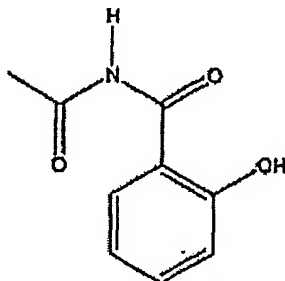
Still additional pharmaceutical agents which may be used in conjunction with this invention include the following materials.



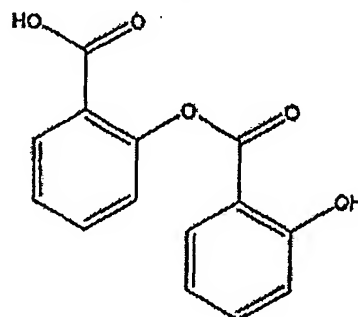
Salicylamide
(Analgesic)



Salicylanilide
(Antifungal)

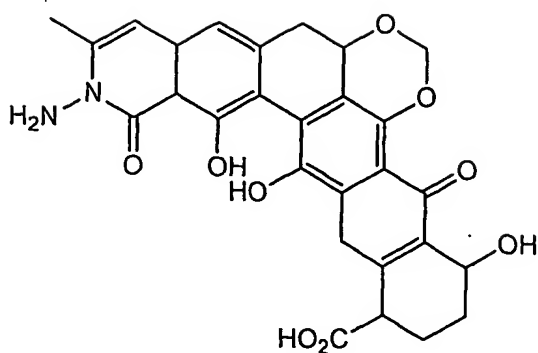


Salacetalamide
(Antipyretic)



Salsalate
(Anti-inflammatory)

18



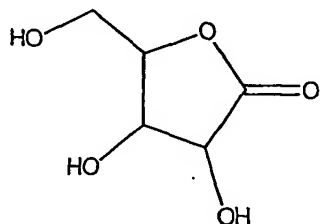
Albofungin
(Antifungal Antibiotic)

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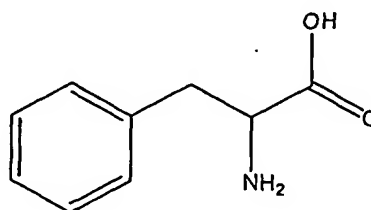
In a similar manner to the previous systems, examples of nutraceutical agents with the desired functional moieties were evaluated for their propensity to

bind to alumina particles. Examples of such compounds were ascorbic acid (Vitamin C) and phenylalanine (sweetener found in Equal®). The structural equations for these materials and their ability to bind to such particles was demonstrated as can be seen in the table which follows:

5



Ascorbic Acid



Phenylalanine

10

SAMPLEUV-VIS ABSORPTION (nm)

15	Ascorbic Acid in water	266
	Ascorbic Acid/SN-AK	260
	Phenylalanine in water	230
20	Phenylalanine/SN-AK	224*

*= The structure of the peak changed in addition to the shift.

It should be noted here that a shift in the absorption maximum was observed on addition of SNOWTEX-AK to the ascorbic acid solution, however a blue shift was observed (hypsochromatic). This shift was due to binding, as no shift was observed when dilute acid was added to a separate solution of ascorbic acid. In a similar way, a blue shift (hypsochromic shift) was also observed with the phenylalanine binding to SNOWTEX-AK.

**Examples of Adsorption of Various Pharmaceutical or Nutritional Materials
to Carrier Nanoparticles and the Selective Release of Such Materials Upon
Occurrence of a Triggering Mechanism:**

In a further set of examples, pharmaceutical materials were adsorbed to carrier alumina particles and then selectively released from the carrier particles. In particular, separate 50 ml Solutions of tetracycline and hydrocortisone agents (0.01 g) in water were prepared to which the alumina nanoparticle (SNOWTEX-AK) suspension (5 ml of 20% wt/wt) were added. A bathochromic shift (red shift) in the UV-VIS Lambda maxima was again observed, indicating strong binding of these pharmaceutical agents to the surface of the alumina particle. The following Table shows the shift in the UV-VIS spectra recorded. Once the pharmaceutical agents had been bound to particles, they were selectively released by a controlled pH trigger mechanism. Thus, by changing the pH of the modified nanoparticle suspension to high pH values, the pharmaceutical agent was released as observed by a second red shift of the UV-VIS Lambda Maxima. In particular, the alkaline agent, dilute sodium hydroxide (0.1N), was added in 0.5 ml amounts to the samples. The tetracycline was released from the alumina surface when the suspension of modified nanoparticles was altered to pH 9/10 or greater. The noted shifts correspond to the absorption maximum of the free pharmaceutical agents.

<u>SAMPLE</u>	<u>UV-VIS ABSORPTION (nm)</u>
Hydrocortisone In water	241
Hydrocortisone/SN-AK	234
Hydrocortisone/SN-AK with Base	244
Hydrocortisone with base	244
Tetracycline In water	357
Tetracycline/SN-AK	365
Tetracycline/SN-AK with base	385
Tetracycline with base	385

Therefore, these two examples of pharmaceutical agents demonstrate the capability of selectively releasing pharmaceutical agents from the carrier particles.

By the use of a "pH trigger" the functional compounds can be released in a controlled manner when needed.

It should be noted that such triggering of the delivery system may be accomplished through environmental changes such as infection which results in pH changes, taking advantage of inherent differences in pH depending on body locations, and the intentional act of introducing chemistries such as pH altering materials to the delivery systems to trigger the release of functional compounds. Chemistries that may be introduced to a delivery system include bicarbonates, carbonates and buffering salts which would result in a pH change on becoming wet with water or biological fluid.

In still a further alternative embodiment, a signal agent, such as a fragrance, may be used by itself or in conjunction with a health related compound on a variety of particle types to both treat a condition, and also to provide an indication to the patient of the effectiveness of such treatment or the occurrence of a particular event. As an example, a fragrance may be adsorbed to one type of particle and an antibiotic may be adsorbed to a second type of particle. The particles can be delivered to an infected site simultaneously. If the infected site is alkaline, it will prompt the release of the antibiotic. Upon removal of the infection, and the return to a more normal acidic environment, the fragrance may be released, thereby providing an indication of the effective treatment of the infection. In a further example, the signal can be used to generate an indication of a particular event, such as the release of body fluids or exudates as in a bandage or personal care product, such as a feminine care product or child care diaper product.

A method used to prepare alumina nanoparticles having functional compounds bonded to the surface included the following steps.

The functional compound was dissolved in water with stirring. To this stirred solution was slowly added the alumina nanoparticles and the resulting mixture stirred for about 5 to 10 minutes to allow the functional compound to bond to the surface of the nanoparticle. The UV-VIS spectrum of the water solution was obtained by taking an aliquot of the stirred mixture and placing it in a quartz cell. The UV-VIS spectra were obtained using a UV-VIS spectrophotometer Model UV-1601 (Shimadzu Corporation) with water as a reference. Zeta Potential and

particle size measurements were determined using a ZetaPals Instrument (Brookhaven Instrument Company, Holtsville, NY).

A method used to release the bonded functional compound utilizing a pH trigger included the following steps. The alumina nanoparticle having the functional agent bonded to the surface was placed in an aqueous solution (suspension) with stirring. To this stirred suspension was slowly added dilute sodium hydroxide (0.1N) dropwise and the pH was subsequently measured. An aliquot of this suspension was taken and the UV-VIS spectrum measured. In this manner, the bonded functional agent's Lambda max peak can be observed to decrease with the free functional agent's Lambda max peak observed to appear and increase.

In yet another embodiment, the delivery system would be incorporated into a tampon. Normal healthy vaginal fluid is acidic, typically in the 3-5 pH range. However, when infected with a yeast infection or other microbial infection, the pH changes to the basic range. This swing in pH would trigger the release of medication such as tetracycline or buffering agents to restore the healthy pH of the vaginal fluid and flora. For instance, a medicated tampon may include a bound antibiotic ("bound" meaning the functional compound adsorbed to the surface of nanoparticles which are themselves attached through charge attraction to a tampon substrate). When the pH of a patient's vagina turns alkaline as a result of a yeast infection, the tampon would be triggered to release the bound antibiotic to control the yeast infection, thereby resulting in the pH returning to the normal acidic environment. In still a further alternative embodiment, such nanoparticle delivery systems may be employed to carry the pharmaceutical agent through the stomach (having an acidic environment) and then release the agents into the small intestine (having a basic/alkaline environment). In still a further alternative embodiment, such nanoparticle delivery systems may be triggered upon the appearance of moisture or body exudates, or application of a pH changing chemistry. In these situations, functional materials contained on carrier nanoparticles on a bandage can be selectively released into or onto a wound site.

Examples of Signal Systems Which Can be Used to Indicate the Release of Pharmaceutical Agents Upon a Change in Environmental Condition:

Silica Particle Binding and Release:

5 The following examples illustrate the use of silica nanoparticles (as opposed to alumina particles) and the bonding of signal functional agents to the surface of the particles. The pH triggered release for silica coated particles is activated by adding acid and lowering the pH to the environment of the silica particles . Dilute acid is used in these examples.

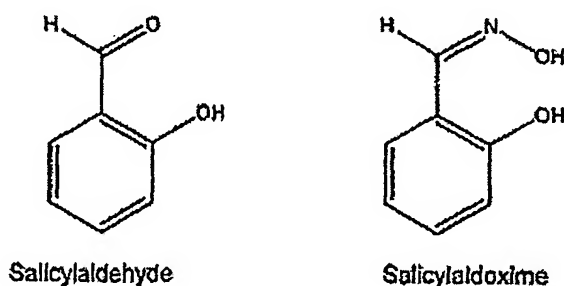
10 A method used to prepare silica nanoparticles having functional agents bonded to the surface included the following steps. The functional agent was dissolved into water with stirring. To this stirred solution was slowly added the silica nanoparticles and the resulting mixture stirred for about 5 to 10 minutes to allow the functional agent to bond to the surface of the nanoparticles. The UV-VIS
15 spectrum of the water solution was obtained by taking an aliquot of the stirred mixture and placing it in a quartz cell. The UV-VIS spectra were obtained using the UV-VIS spectrophotometer Model UV-1601 with water as a reference. Zeta Potential and particle size measurements were determined using a ZetaPals Instrument (Brookhaven Instrument Company, Holtsville, NY).

20 A method used to release the bonded functional agent from the silica surface using a pH trigger included the following steps. The silica nanoparticle having the functional agent bonded to the surface was placed in aqueous solution (suspension) with stirring. To this stirred suspension was slowly added dilute hydrochloric acid (0.1N) dropwise and the pH measured. An aliquot of this
25 suspension was taken and the UV-VIS spectrum measured. In this manner, the bonded functional agent's Lambda max peak can be observed to decrease with the free functional agent's Lambda max peak observed to appear and increase.

 In a similar fashion, the binding of active fragrance compounds to silica nanoparticles (SNOWTEX C, Nissan Chemicals America, Houston, TX) was
30 demonstrated. Accordingly, to a solution (0.01g of salicylaldehyde in 50 ml of water) of salicylaldehyde (used in the perfume industry as a base fragrance) was added a dilute suspension (3 ml of 2% wt/wt) of silica nanoparticles (Snowtex C,

Nissan Chemicals America, Houston TX) with stirring. The UV-VIS absorption of the salicylaldehyde underwent a red shift in its lambda max (see the table below) and the characteristic fragrance disappeared. The red shift is characteristic of the binding of the aryl aldehyde functionality to the silica surface. Upon addition of dilute acid (hydrochloric acid as stated), the aldehyde was released and the fragrance returned. The UV-VIS absorption also underwent a blue shift to return to that of the starting aldehyde. Such chemistry may be used in conjunction with a pharmaceutical to be released upon the change of an environmental condition to indicate/signal that the pharmaceutical material has been delivered. For instance, such signal agent may be adsorbed onto a silica particle. A pharmaceutical compound may be separately adsorbed onto an alumina particle. The particles may be combined and jointly used within a delivery vehicle or as part of a modified drug delivery device. The functional agents then would be triggered upon the occurrence of separate chemical events.

In a similar manner, salicylaldoxime a metal sequestering agent, was also found to bind to the silica particle surface and undergo a pH triggered release. The structural equations and exemplary data are illustrated in the following table.



<u>SAMPLE</u>	<u>UV-VIS Absorption (nm)</u>	
	<u>After Addition of Silica</u>	<u>After Addition of Acid</u>
Salicylaldehyde 327nm	382	327
Salicylaldoxime 303nm	350	340

Additionally, a titration study using UV-VIS spectroscopy was carried out to determine the pH at which all of the salicylaldehyde was released. This was found to be at pH 6.

In additional alternative embodiments, following being affixed to such substrates, upon exposure to a change in condition (such as pH) the functional compounds would be released from the substrate, but the particles would be left behind.

5 In a specific embodiment, carrier particles (and desirably nanoparticles, that is particles having sizes of less than about 1 micron in size, more desirably between about 5 nm and 500 nm in size, and even more desirably, between about 10 nm – 200 nm in size) including pharmaceutical compounds, can be applied to a topical bandage by various application methods. The application methods may
10 include a gel, a water suspension, a dry coating or a powder placed between the layers of the bandage if the particles are included in a vehicle for ease of application. The bandage can then be dried, if appropriate, whereby the charges of the particles would maintain them in close association with the bandage substrate.

15 It should be recognized that the bound pharmaceutical or nutritional chemistry could be used with or without triggerable release. Alternatively, some of the bound chemistry in a multiple chemistry particle system could be triggerably releasable, while other bound chemistry could be intentionally retained on the carrier particles. In this fashion, the bound chemistry could perform its
20 advantageous function while still being attached to the carrier particles, for ease of removal or to lower the potential toxicity of the functional agent/compound. An example of such usage would be using a bound salicylaldoxime to remove heavy metals from the body or waste water without the loss of or exposure to the free complexing agent.

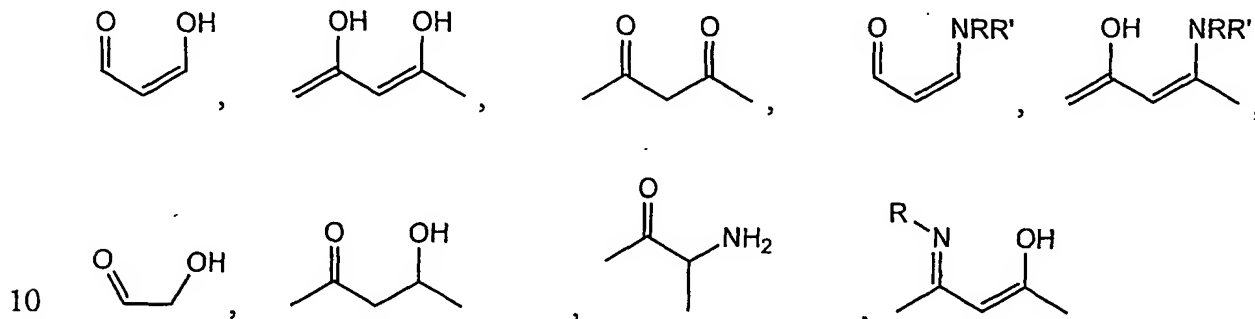
25 In another example, tetracycline could function as an antibiotic while still being bound on a particle. This could allow the antibiotic to function in the stomach and intestines without crossing over into the bloodstream of a patient (because of the size of the particle). This control of the antibiotic release could assist with lowering the risk of sensitization of patients who are allergic to such
30 medications.

These and other modifications and variations to the present invention may be practiced by those of ordinary skill in the art, without departing from the spirit and scope of the present invention, which is more particularly set forth in the

appended claims. In addition, it should be understood that aspects of the various embodiments may be interchanged both in whole or in part. Furthermore, those of ordinary skill in the art will appreciate that the foregoing description is by way of example only, and is not intended to limit the invention so further described in such
5 appended claims.

What Is Claimed:

1. A composition of matter comprising:
 - a particle containing alumina, at least a portion of the alumina being present on a surface of the particle; and
 - 5 a functional compound bonded to the alumina on the surface of the particle, the functional compound prior to bonding with the alumina containing a moiety comprising:



or a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group.

2. A composition as defined in claim 1, wherein the particles containing alumina bonded to the functional compound are positively charged.
3. A composition as defined in claim 1, wherein the particle consists essentially of alumina.
4. A composition as defined in claim 1, wherein the particle comprises a core material coated with alumina.
5. A composition as defined in claim 4, wherein the core material comprises silica.
6. A composition as defined in claim 1, wherein the functional compound comprises a UV absorber, a pharmaceutical, an odor control agent, a fragrance, a therapeutic agent, a nutraceutical agent, an anti-bacterial agent, an anti-microbial agent, an anti-viral agent, or a xenobiotic.
7. A composition as defined in claim 1, wherein the particle containing alumina bonded to the functional compound has an average dimension of less than about 1 mm.

8. A composition as defined in claim 1, wherein the particle containing alumina bonded to the functional compound has an average dimension of less than about 100 microns.

9. A composition as defined in claim 1, wherein the particle containing alumina bonded to the functional compound has an average dimension of less than about 1,000 nm.

10. A composition as defined in claim 1, wherein the functional compound comprises hydrocortisone.

11. A composition as defined in claim 1, wherein the functional compound comprises ascorbic acid.

12. A composition as defined in claim 1, wherein the functional compound comprises aspartame.

13. A composition as defined in claim 1, wherein the functional compound comprises a cyclomycin.

14. A composition as defined in claim 1, wherein the functional compound comprises tetracycline.

15. A composition as defined in claim 1, wherein the particles are amorphous.

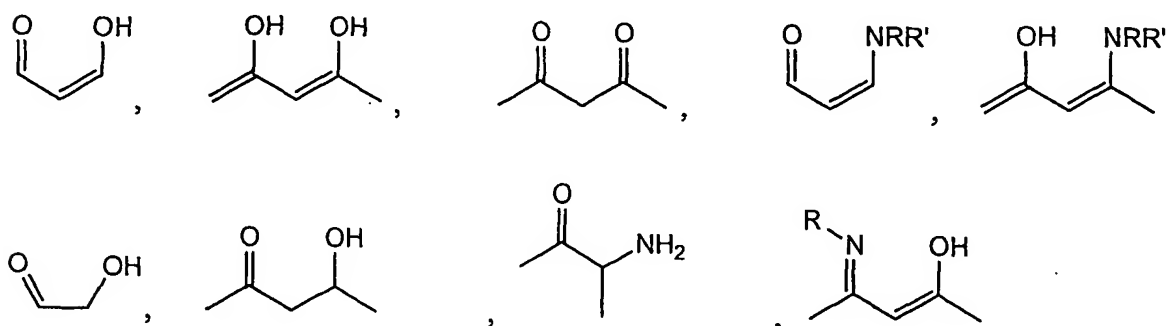
16. A composition as defined in claim 1, wherein the particle containing alumina bonded to the functional compound has a zeta potential of at least 20 mV.

17. A composition as defined in claim 1, wherein at least two functional compounds are bonded to the alumina.

18. A composition as defined in claim 1, wherein the functional compound comprises a colorant.

19. A composition as defined in claim 1, wherein the composition comprises a plurality of the particles containing alumina bonded to the functional compound contained in a liquid vehicle.

20. A nanoparticle for a printing process comprising:
 a particle containing alumina, at least a portion of the alumina being present on a surface of the particle; and
 a colorant compound bonded to the alumina on the surface of the particle, the colorant compound prior to bonding with the alumina containing a moiety comprising:



10

or a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, and aryl group.

21. A nanoparticle as defined in claim 20, wherein the particles containing alumina bonded to the colorant compound are positively charged.
22. A nanoparticle as defined in claim 20, wherein the particle consists essentially of alumina.
23. A nanoparticle as defined in claim 20, wherein the particle comprises a core material coated with alumina.
24. A nanoparticle as defined in claim 23, wherein the core material comprises silica.
25. A nanoparticle as defined in claim 20, wherein the nanoparticle has an average dimension of less than about 1,000 nm.
26. A nanoparticle as defined in claim 20, wherein the nanoparticle has an average dimension of less than about 500 nm.
27. A nanoparticle as defined in claim 20, wherein the particle containing alumina bonded to the colorant compound has a zeta potential of at least 20 mV.
28. A nanoparticle as defined in claim 20, wherein the alumina and the colorant compound both have a positive zeta potential.
29. A nanoparticle as defined in claim 20, wherein the alumina on the surface of the particle is further bonded to a functional additive.

30. A nanoparticle as defined in claim 29, wherein the functional additive comprises a charge carrier, a thermal oxidation stabilizer, a viscoelastic property modifier, a cross-linking agent, a plasticizer, a charge control additive, a flow control additive, a filler, a surfactant, a chelating agent, a leuco dye, and colorant stabilizer, or a combination thereof.

31. A nanoparticle as defined in claim 20, wherein the colorant compound comprises a dye.

32. A nanoparticle as defined in claim 31, wherein the dye contains an anthraquinone chromophore.

33. A nanoparticle as defined in claim 31, wherein the dye contains salicylate or 3-hydroxy-2-naphthoic acid moieties.

34. A nanoparticle as defined in claim 31, wherein the dye is based on chromotropic acid.

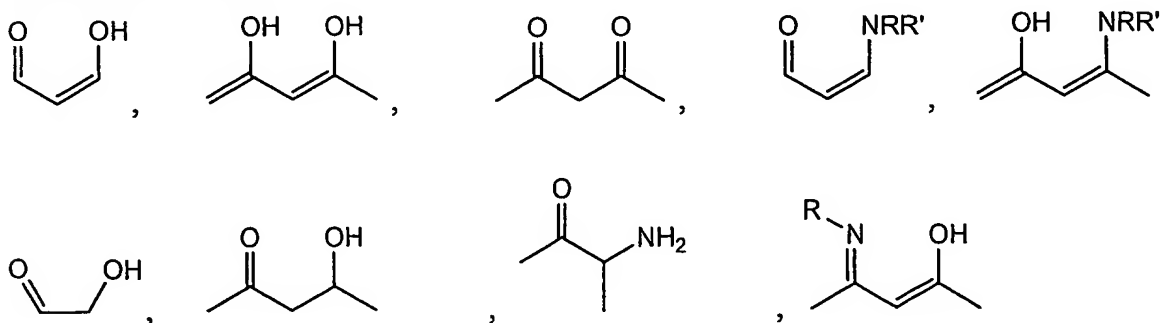
35. A nanoparticle as defined in claim 31, wherein the dye contains acetoacetanilide.

36. A nanoparticle as defined in claim 31, wherein the dye contains a naphthoquinone.

37. A nanoparticle as defined in claim 31, wherein the dye comprises a mordant dye.

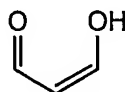
38. A nanoparticle as defined in claim 31, wherein the dye comprises CI Mordant Red 7 or Eriochrome Red B.

39. A recording medium comprising:
 a plurality of particles containing alumina, at least a portion of the
 alumina being present on a surface of the particles;
 a colorant compound bonded to the alumina on the surface of the
 particle, the functional compound prior to bonding with the alumina containing a
 moiety comprising:



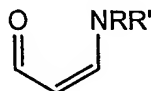
or a tautomer thereof, or a functional equivalent thereof and wherein R and R'
 comprise independently hydrogen, an alkyl group, or an aryl group; and
 a liquid vehicle.

40. A recording medium as defined in claim 39, wherein the colorant
 compound contained the moiety:



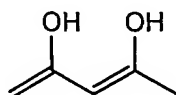
or a tautomer.

41. A recording medium as defined in claim 39, wherein the colorant
 compound contained the moiety:



and wherein R and R' are hydrogen.

42. A recording medium as defined in claim 39, wherein the colorant
 compound contained the moiety:



or a tautomer.

43. A recording medium as defined in claim 39, wherein the particles
 consist essentially of alumina.

44. A recording medium as defined in claim 39, wherein the particles comprise a core material coated with an alumina.

45. A recording medium as defined in claim 44, wherein the core material comprises silica.

5 46. A recording medium as defined in claim 39, wherein the particles have an average dimension of less than about 1,000 nm.

47. A recording medium as defined in claim 39, wherein the particles containing the alumina bonded to the colorant compound has a zeta potential of greater than about 20 mV.

10 48. A recording medium as defined in claim 39, wherein the alumina and the colorant compound together have a positive zeta potential.

49. A recording medium as defined in claim 39, wherein the colorant compound comprises a dye.

15 50. A recording medium as defined in claim 49, wherein the dye contains an anthraquinone chromophore.

51. A recording medium as defined in claim 49, wherein the dye contains salicylate or 3-hydroxy-2-naphthoic acid moieties.

52. A recording medium as defined in claim 49, wherein the dye is based on chromotropic acid.

20 53. A recording medium as defined in claim 49, wherein the dye contains acetoacetanilide.

54. A recording medium as defined in claim 49, wherein the dye contains a mordant dye.

25 55. A recording medium as defined in claim 49, wherein the dye is CI Mordant Red 7.

56. A recording medium as defined in claim 49, wherein the dye contains a naphthoquinone.

30 57. A printing process comprising ejecting the recording medium of claim 39 in the form droplets from an orifice in according with a recording signal to form an image on a substrate.

58. The printing process of claim 57, wherein the substrate comprises a woven fabric, a non-woven fabric, a polymeric film, glass, or a paper.

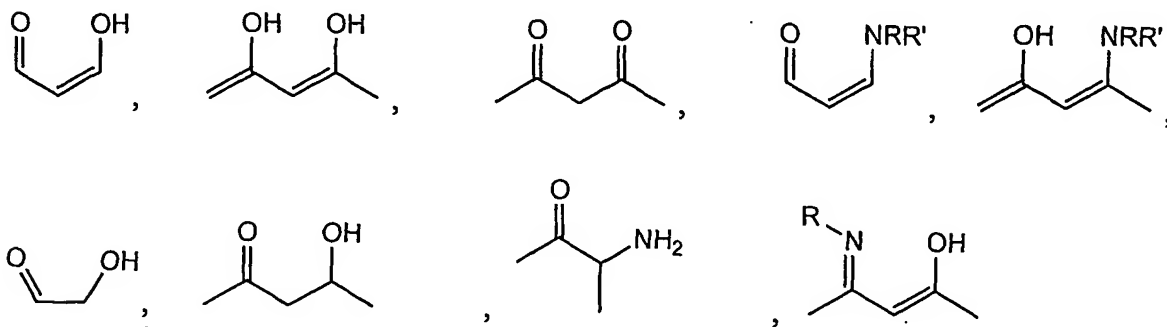
59. The printing process of claim 57, wherein the process is an ink-jetting process.

60. An article of manufacture comprising:

a substrate having a receiving surface containing negative charges;

5 and

a plurality of positively charged particles bonded to the receiving surface of the substrate through coulombic attraction, the particles containing alumina, at least a portion of the alumina being present on a surface of the particles, and wherein a functional compound is bonded to the alumina on the surface of the particle, the functional compound prior to bonding with the alumina containing a moiety comprising:



15

or a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group.

61. An article as defined in claim 60, wherein the particle comprises a core material coated with alumina.

20 62. An article as defined in claim 60, wherein the core material comprises silica.

63. An article as defined in claim 60, wherein the functional material comprises a colorant, a UV absorber, a pharmaceutical, an odor control agent, a fragrance, a therapeutic agent, a nutraceutical agent, an anti-bacterial agent, an anti-microbial agent, an anti-viral agent, or a xenobiotic.

25

64. An article as defined in claim 60, wherein the particle containing alumina bonded to the functional compound has an average dimension of less than about 1 mm.

65. An article as defined in claim 60, wherein the particle containing alumina bonded to the functional compound has an average dimension of less than about 1,000 nm.

66. An article as defined in claim 60, wherein the functional compound
5 comprises hydrocortisone, ascorbic acid, or aspartame.

67. An article as defined in claim 60, wherein the functional compound comprises tetracycline.

68. An article as defined in claim 60, wherein the particle containing alumina bonded to the functional compound has a zeta potential of at least 20 mV.

10 69. An article as defined in claim 60, wherein the plurality of particles are contained within a liquid vehicle when applied to the substrate.

70. An article as defined in claim 60, wherein the functional compound comprises a dye.

71. An article as defined in claim 70, wherein the substrate comprises a
15 woven or non-woven material comprising synthetic polymeric fibers.

72. An article as defined in claim 71, wherein the substrate is subjected to a corona treatment prior to bonding with the plurality of positively charges particles.

73. An article as defined in claim 71, wherein the substrate is subjected
20 to an electret treatment prior to bonding with the plurality of positively charges particles.

74. An article as defined in claim 71, wherein the article has been exposed to microwave radiation or radio frequency radiation after the substrate and the plurality of charged particles have been bonded together.

25 75. An article as defined in claim 70, wherein the substrate comprises natural fibers carrying the negative charges.

76. An article as defined in claim 75, wherein the natural fibers comprise cotton or cellulose fibers.

77. An article as defined in claim 70, wherein the dye contains an
30 anthraquinone chromophore.

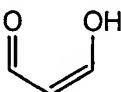
78. An article as defined in claim 70, wherein the dye contains salicylate or 3-hydroxy-2-naphthoic acid moieties.

79. An article as defined in claim 70, wherein the dye is based on chromotropic acid.

80. An article as defined in claim 70, wherein the dye contains acetoacetanilide.

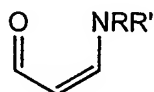
5 81. An article as defined in claim 70, wherein the dye contains a naphthoquinone.

82. An article as defined in claim 70, wherein the colorant compound contained the moiety:



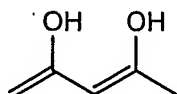
10 or a tautomer of this moiety.

83. An article as defined in claim 70, wherein the colorant compound contained the moiety:



and wherein R and R' are hydrogen.

15 84. An article as defined in claim 70, wherein the colorant compound contained the moiety:



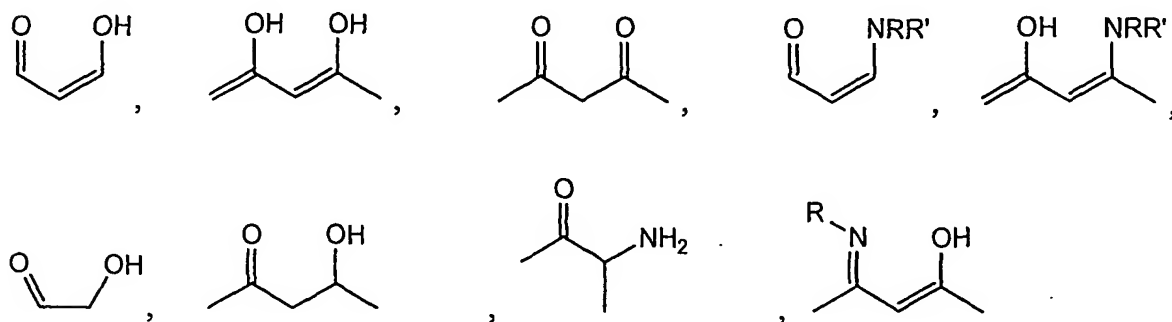
or a tautomer of this moiety.

20 85. An article as defined in claim 70, wherein the plurality of particles have an average dimension of less than about 1,000 nm.

86. An article as defined in claim 60, wherein the receiving surface of the substrate and the particles have a surface charge difference of at least 42 mV.

25 87. An article as defined in claim 70, wherein the receiving surface of the substrate and the particles have a surface charge difference of at least 42 mV.

88. A method of making a composition of matter comprising:
 providing a plurality of particles, the particles containing alumina, at
 least a portion of the alumina being present on a surface of the particles; and
 bonding to the alumina on the surface of the particles a functional
 5 compound, the functional compound prior to bonding with the alumina containing a
 moiety comprising:



10

or a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group.

89. A method as defined in claim 88, wherein the particle consists essentially of alumina.

15 90. A method as defined in claim 88, wherein the particles comprise a core material coated with an alumina.

91. A method as defined in claim 90, wherein the core material comprises silica.

20 92. A method as defined in claim 88, wherein the functional material comprises a colorant, a UV absorber, a pharmaceutical, an odor control agent, a fragrance, a therapeutic agent, a nutraceutical agent, an anti-bacterial agent, an anti-microbial agent, an anti-viral agent, or a xenobiotic.

25 93. A method as defined in claim 88, wherein the particle containing alumina bonded to the functional compound has an average dimension of less than about 1 mm.

94. A method as defined in claim 88, wherein the particle containing alumina bonded to the functional compound has an average dimension of less than about 1,000 nm.

30 95. A method as defined in claim 89, wherein the functional compound comprises hydrocortisone, ascorbic acid, or aspartame.

96. A method as defined in claim 88, wherein the functional compound comprises tetracycline.

97. A method as defined in claim 88, wherein the particles are amorphous.

5 98. A method as defined in claim 88, wherein the particle containing alumina bonded to the functional compound has a zeta potential of at least 20 mV.

99. A method as defined in claim 88, wherein at least two functional compounds are bonded to the alumina.

10 100. A method as defined in claim 88, further comprising the step of combining the particles bonded with the functional compound with a liquid vehicle.

101. A method as defined in claim 100, wherein the composition comprises an ink composition.

102. A method as defined in claim 88, wherein the functional compound comprises a dye.

15 103. A method as defined in claim 102, wherein the dye contains an anthraquinone chromophore.

104. A method as defined in claim 102, wherein the dye contains salicylate or 3-hydroxy-2-naphthoic acid moieties.

20 105. A method as defined in claim 102, wherein the dye is based on chromotropic acid.

106. A method as defined in claim 102, wherein the dye contains acetoacetanilide.

107. A method as defined in claim 102, wherein the dye contains a naphthoquinone.

25

108. A method of utilizing a triggerably releasable delivery system in the treatment of a patient's body comprising:

a) providing at least one type of particle selected from alumina particles, alumina covered particles, and silica particles;

5 b) adsorbing at least one functional compound to the surface of the particle or particles to form at least a partially coated particle or particles;

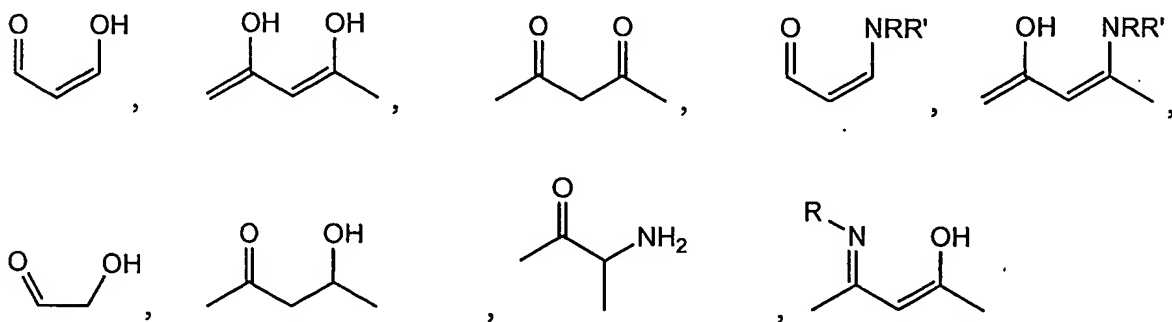
c) exposing the at least partially coated particle or particles to a patient's body;

10 d) exposing the particle or particles to an environmental or chemical condition whereby the health related compound is released from the surface of the particle to the patient's body.

109. The method of claim 108 wherein the environmental or chemical condition is selected from the group consisting of a chemical trigger, a change in pH, introduction of the particle to moisture or body exudates.

15 110. The method of claim 108 wherein multiple types of particles are coated with functional compounds.

111. The method of claim 108 wherein the particles contain alumina, at least a portion of the alumina being present on a surface of the particles; and the functional compound prior to adsorbing with the alumina particle containing a moiety comprising:



or a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group.

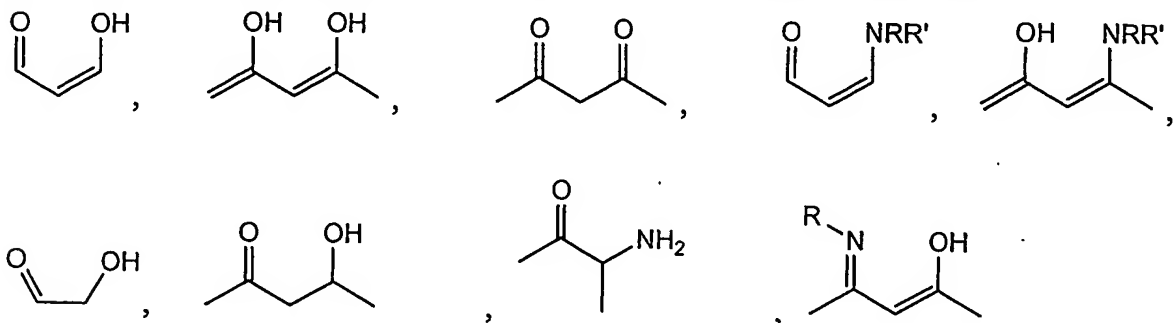
112. A triggerable delivery system comprising:

a particle; and

a health-related compound adsorbed to the surface of said particle, said health-related compound capable of being released from said particle upon either
5 exposure to a change in pH, moisture, chemical stimuli, or body exudates.

113. The triggerable delivery system of claim 112 wherein the particle contains alumina, at least a portion of the alumina being present on a surface of the particle; and

the health related compound, prior to being adsorbed with the
10 alumina on the surface of the particle containing a moiety comprising:



15 or a tautomer thereof, or a functional equivalent thereof and wherein R and R' comprise independently hydrogen, an alkyl group, or an aryl group.

114. A drug delivery device including a triggerable delivery system, said triggerable delivery system comprising a particle; and
a health-related compound adsorbed to the surface of said particle, said health-
20 related compound capable of being released from said particle upon either exposure to a change in pH, moisture, chemical stimuli, or body exudates.